SUPPORT FOR THE AMENDMENTS

Claims 6, 7, 15, 19, 23, 24, and 28 were previously canceled.

Claims 2-5, 8, 9, 11, 20-22, 31, 39, and 59 are canceled herein.

Claims 1, 10, 12, 14, 16-18, 32-35, 37, 38, 40-43, 48-55, and 58 have been amended.

The amendment of Claims 1, 10, 12, 14, 16-18, 32-35, 37, 38, 40-43, 48-55, and 58 is supported by the corresponding claims as previously presented and originally filed, as well as page 5, lines 17-19 of the specification.

No new matter has been added by the present amendments.

REMARKS

Claims 1, 10, 12-14, 16-18, 25-27, 29, 30, 32-38, 40-58, and 60 are pending in the present application.

The rejection of Claims 1, 2, 4, 8-10, 12-14, 16-18, 27, 33, 36, 37, 43-49, and 55-57 under 35 U.S.C. §102(b) over Gefter et al (US 6,180,608) is obviated by amendment.

The present invention relates to a sustained release pharmaceutical administration form, as well as methods and kits, where the form is a pharmaceutical gel preparation containing D-63153. As the Examiner recognizes, Gefter et al fails to disclose or suggest D-63153.

The standard for determining anticipation requires that the reference "must teach every element of the claim" (MPEP §2131). Accordingly, Gefter et al does not anticipate the claimed invention.

Applicants request withdrawal of this ground of rejection.

The rejections of: (a) Claims 11, 20-22, 25-26, 29-32, and 34-35 under 35 U.S.C. §103(a) over Gefter et al in view of Bauer et al; and (b) Claims 38-42 and 58-60 under 35 U.S.C. §103(a) over Gefter et al in view of Bauer et al and Engel et al, are obviated in part by amendment and traversed in part.

The present invention relates to a sustained release pharmaceutical administration form, as well as methods and kits, where the form is a pharmaceutical gel preparation containing D-63153. As the Examiner recognizes, Gefter et al fails to disclose or suggest D-63153.

Indeed, Gefter et al provides the therapeutic effectiveness of a pharmaceutically active peptide which seeks to be maintained *in vivo* over prolonged time periods to treat hormone-

dependent diseases. To this end, Gefter et al disclose a pharmaceutical composition comprising a water-insoluble complex composed of a peptidic compound and a macromolecule carrier that allows for sustained release of the peptidic compound in vivo upon administration of the complex. The peptidic compound of Gefter et al comprises peptides, polypeptides and proteins. The peptidic compound can also comprise an LHRH analogue which may be an LHRH agonist or an LHRH antagonist in a narrower sense, including the exemplary the LHRH antagonists PPI-149, PPI-258 and cetrorelix.

In Gefter et al, the carrier macromolecule comprises cationic carrier macromolecule like poly-L-lysine and other polymers of basic amino acids or anionic carrier macromolecule like polyalcohol derivatives, specifically polysaccharides and more specifically carboxymethylcellulose, algin, alginate, acetate polymers, acrylic polymers, alkali starch glycolate and others.

The current invention does not comprise a carrier macromolecule and does not use such carrier macromolecule. On the contrary the inventive peptide forms the administration form for sustained release itself.

Gefter et al use a 0.9% sodium chloride in Example 14 as a reconstitution vehicle to reconstitute the complex PPI-149-CMC, consisting of the peptidic compound PPI-149 and the macromolecule carboxymethylcellulose, wherein the complex PPI-149-CMC is already a sustained delivery complex. However, the present invention uses sodium chloride as an inorganic salt as the reconstitution medium and to prepare a sustained release form from an easily soluble peptide or peptide salt.

In addition to acknowledging that Gefter et al fails to disclose or suggest D-63153, the Examienr recognizes that Gefter et al also discloses differing sodium chloride concentrations (Official Action page 8, numbered paragraph 14). However, the Examiner alleges that Bauer

et al disclose a pharmaceutical administration form containing peptides prone to aggregation in the form of their acetate, gluconate, glucuronate, lactate and others.

Bauer et al discloses that peptides have a nature prone to uncontrolled aggregation and that the peptides if administered lead to a concentration-dependent lowering of the bioavailability from the peptide concentration. Bauer at al therefore disclose that addition of a free acid to the easily soluble peptide salt prevents that peptide salts prone to aggregation. The combination of the teaching of Gefter et al and of Bauer et al does not lead to the inventive subject matter.

Moreover, as recognized by the Examiner, Bauer et al does not actually disclose or suggest D-63153. The Examiner cites paragraph [0014] of Bauer et al, which states "The peptides employed are the LHRH antagonists antide, A-75998, ganirelix and Nal-Glu antagonist, but in particular cetrorelix, antarelix, and the antagonists according to the U.S. Pat. No. 5,942,493 and DE 19911771.3." These references disclose a large number of peptides, one of which is D-63153. However, Bauer et al or these references fail to provide any specific motivation to select D-63153 for use as presently claimed.

Applicants submit that, at best, even if the artisan were to combine the disclosure of Gefter et al and Bauer et al, the combination would provide and "invitation to experiment" or could be viewed as making it "obvious to try" to arrive at the present invention. However, "obvious to try" has long been held not to constitute obviousness. *In re O'Farrell*, 7 USPQ2d 1673, 1680 81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 [82 USPQ2d 1385](2007) does not eliminate the "obvious to try is not obvious" standard, as it clearly states that "obvious to try" may constitute obviousness, but only under certain circumstances. Specifically, KSR

stated that the fact that a claimed combination of elements was "obvious to try" might show that such combination was obvious under 35 U.S.C. § 103, since, if there is design need or market pressure to solve problem, and there are finite number of identified, predictable solutions, person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation.

The Examiner offers a series of conclusionary statements on page 10 with respect to an alleged desire to substitute the antagonists used in the cited art with D-63153 and that the results would be expected. However, the Examiner offers nothing to show how the *KSR* factors apply and how the results set forth in the Examples of the present application would be expected or anticipated success. Therefore, the Examiner fails to make out a sufficient prima facie case of obviousness and the data in the specification rebuts the same.

Applicants wish to further note that the Examiner emphasizes that Bauer et al disclose a pharmaceutical administration form which contains peptides prone to aggregation. Bauer et al provide a teaching to *avoid aggregation* of the peptides whereas the presently claimed invention is a sustained release formulation and consequently involves the aggregation of peptides by reconstitution of lyophilized peptide salts with anorganic salts or acetic acid salts. Thus, the mechanism by which the claimed invention is achieved as compared to the cited are at direct odds and are incompatible. Therefore, Applicants submit that the teachings of Bauer et al are not relevant to the claims of the present application. It is only when Applicants disclosure is used as a guidepost to reconstitute the claimed invention with the benefit of hindsight that the disclosure of Geftner et al and Bauer et al are combinable. In all other proper circumstances, the skilled artisan would not find modification in the disclosure of Bauer et al to modify the disclosure of Geftner et al. Thus, the claimed invention is not obvious in view of the combined disclosures of Geftner et al and Bauer et al.

In a further consideration the Examiner refers to the Engel et al, and alleges that the current invention in claims 38-42 and 58-60 is obvious. Applicants disagree.

Engel et al teach a kit comprising an initial dose of an LHRH antagonist and at least one maintenance dose of the same LHRH antagonist for the treatment of hormone-dependent conditions. The current invention claims in claims 38-42 and 58-60 relate a kit comprising an LHRH antagonist as finished preparation of the peptide compound and a solution of an inorganic salt or acetic acid salt for reconstitution. In view of the foregoing, the combination of the teaching of Gefter et al, Bauer et al, and of Engel et al does not lead to the inventive subject matter of the kit claims.

Applicants request withdrawal of these grounds of rejection.

Applicants respectfully submit that the above-identified application is now in condition for allowance. Early notification to this effect is earnestly solicited.

Respectfully submitted,

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